research teams; and the brave patients with NSCLC and their caregivers who participated in this study.

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Discussion

Dr Erino Rendina *(Rome, Italy)*. Your results are remarkable, but the remarkability in terms of AEs also depends on the selection of your patients. In fact, I think when the patients have an FEV_1 of approximately 50% and no other exclusion criteria, lobectomy could still be done, and this remains the gold standard because it's also preserving the quality of life. Nonetheless, looking specifically at the data you presented here, I agree with your conclusion that SR can be undertaken safely in high-risk patients with NSCLC with acceptable 30- and 90-day mortality and morbidity.

In your article, you stated that SR included wedge resection or segmental resection and could be performed by video-assisted thoracic surgery (VATS) or thoracotomy. Potential benefits of thoracoscopic resections have been reported that include equivalent oncologic outcomes to those of open surgery and less morbidity. Do you know what percentage of resections were VATS or open in your group, and did you look at whether it could have an impact on the results?

Dr Fernando. I'm going to take your first point addressing the 50% FEV_1. Our criteria were broad. They included patients who may have had restrictive disease and cardiac disease. One issue to point out is that as a surgeon you may see a patient who has an FEV_1 of 45% in whom you would definitely perform a lobectomy, but you may also see a patient with an FEV_1 of 55% who clearly would not tolerate a lobectomy because of other things. So our criteria were broad, but would still allow the thoracic surgeon to look at each patient and make an assessment that SR was the optimal approach for a specific patient, and allow enrollment in the study.

The second question was with the VATS versus thoracotomy. Some 65% of these patients in both groups actually had a thoracoscopic resection. It was interesting that most of the resections performed were thoracoscopic. I don't know the breakdown in terms of wedge and segment, and whether more segments were done with one approach or the other. That is planned for another analysis. Last year we presented the preliminary data on 150 patients, looking at 30- and 90-day impact on pulmonary function test, and we saw no difference between the VATS and open groups in that particular analysis.

Dr Rendina. You stated that 2 methods of brachytherapy were allowed in your study. Was your choice to use one method or the other dictated by any specific reason?

Dr Fernando. This was really at the discretion of the surgeon. We reviewed the techniques that were out there at the time the study was developed, and there was no data to support one over the other. So we left the decision to the surgeon. We have not analyzed the impact of the brachytherapy approach specifically on complications. There has been a brachytherapy quality control analysis that was presented at ASTRO by one of the radiation oncologists on the protocol, and this looked more at the ability to deliver the dose that was planned, and, again, I don't know the differences between the 2 groups.

Dr Rendina. Are there particular precautions that have to be taken with manipulating this material?

Dr Fernando. I wear lead when I do these procedures. When I'm actually sewing these in place, I don't tie down directly onto the lung. I tie extracorporeally when placing these by VATS or take a clip applier and use the clips as my knot rather than trying to tie with my hand directly onto the mesh.

Dr Rendina. In your report, the 90-day outcomes demonstrated a 2.7% mortality, which is absolutely acceptable considering the greater than average risk of these patients. However, I noticed that 1 death in the SR group included cancer progression, which is pretty surprising for patients with stage I disease. Do you have an explanation for this? Do you want to comment on this issue?

Dr Fernando. I don't know the results of that. As I said, we're planning on presenting the survival and recurrence data when this matures. I don't know whether the patient truly had a recurrence or occult metastatic disease that we didn't know about at the time, and the patient presented a month or so after resection with this. That needs to be looked at a bit more carefully.

Dr Rendina. Thank you.

Dr Thomas Waddell *(Toronto, Ontario, Canada)*. I want to follow up on one point that Dr Rendina made and ask you to talk a bit about the new study that is going to compare this type of treatment with SBRT. This morning we heard Dr Puri talk about an analysis,

which was retrospective, but it seems that the groups treated with SBRT and surgery were very different. Overall, 7% mortality in the surgery group and zero in the SBRT group seems to favor SBRT. So I think that the subject of who should enter these trials is critical. I take your point that you need to have an accruing trial, but I think defining what we mean by high risk is very important. How can we use this information to think about the next trial, that is, to say how do we define a high-risk person? I would say a 30-day mortality of 1.4 is not that different than what Dr Allen reported based on Z0030 for lobectomy. So I would come back to Dr Rendina's point, that I'm not so sure these patients are really as high risk as you would have us believe, and certainly they are not as high risk as the patients who have been up to now dealt with by SBRT.

Dr Fernando. Actually, I would say that some of those patients treated with SBRT are probably good-risk patients as well, who are getting to the radiation oncologists without the benefit of seeing a surgeon and in some cases may have refused surgery. Every patient in this study was seen by an ACOSOG-approved thoracic surgeon, which meant they were board-certified in cardiothoracic surgery, with 50% of their practice devoted to thoracic surgery, or members of the General Thoracic Club, and they had to pass a credentialing test to be involved in this. Every patient had to be seen by a thoracic surgeon who decided if the patient was high risk for lobectomy. We can all say that we operate on patients with an FEV_1 of 40% or 35% and sometimes perform lobectomies on those patients. Every patient has a specific set of comorbidities that allows you as a surgeon to make that judgment. If we had made this trial restrictive and only taken 30% or less or 40% or less, or whatever number we would have chosen, it would have taken twice as long to accrue to this study. This next study is going to be looking at patients with exactly the same set of inclusion criteria. Every patient will have to be seen by a thoracic surgeon. The only difference is that the tissue diagnosis will have to be made up front so we avoid the problem that other SBRT studies have made by including patients who don't have a tissue diagnosis. We are going to have common definitions of outcome, including complications and recurrence, because there are also differences in recurrence rates between the SBRT and surgical studies that can be explained in part by differences of definition. So this next study will give us our best chance to see what the role of surgery is for this group of patients.

Dr Todd Demmy *(Buffalo, NY)*. Do you have any data on the discharge independence of these patients? I think that's the other element that we have to capture when we start thinking about comparative studies. It was already stated this morning in the lecture that if it's less invasive, it tends to win, so SBRT already has an edge on that. Are you going to collect data to show that these patients don't go to nursing homes and end up with a lot of repeat visits beyond the 90-day mortality end point? Are you going to look at these functional and quality of life outcomes?

Dr Fernando. With Z4032, we didn't include that as an end point, but the Z4099 study, which opened last week, the case report forms specifically ask those questions about where the patient goes, home or to an acute care facility. I think that is an important outcome to measure.

Dr Scott Swanson *(Boston, Mass)*. That was an outstanding presentation, and you are to be commended for doing this trial because it's critical for us as surgeons. The outcome data are amazing, really good mortality and morbidity.

Do you have any data on lymph node sampling? I know that's not the point of this study, but as we go forward comparing with SBRT, certainly that is a major difference. Was that part of this study? Was there any requirement? Do you have any details on that?

Dr Fernando. Lymph node counts were not collected in our case report forms. We are planning an analysis comparing VATS and thoracotomy, which Michael Kent from Beth Israel Deaconess is going to lead. We are going to be looking at all the operative and path notes that are available as part of the source data, even though that specific information was not collected in the case report forms up front. We hope to have that information within the next 6 months to present to everybody when we look at the differences for the patients who had VATS or thoracotomy.

Dr Servet Bolukbas *(Wiesbaden, Germany)*. During the evaluation of your patients, there is a high possibility of detecting chronic obstructive pulmonary disease. Were there any attempts to treat those patients with drugs, to send them to pulmonary rehabilitation to improve FEV_1, to switch the patients from high to normal risk?

Dr Fernando. Not specifically in this group. I think the difference between these patients and patients in the National Emphysema Treatment Trial study, for example, is that you don't really have the luxury of 6 weeks to perform pulmonary rehabilitation in these patients. You want to try and deal with the cancer within a reasonable time frame. So we have not been putting patients through pulmonary rehabilitation before resecting lung cancers.

Dr Bolukbas. But in stage I, I think there is time to do pulmonary rehabilitation for 6 weeks.

Dr Fernando. Perhaps.

Dr Joel Cooper *(Philadelphia, Pa)*. Just for point of emphasis, I want to recapitulate. I am concerned with people labeling an FEV_1 of 50% as defining ''high risk'' because it's not, and the pulmonary physicians and radiotherapists are going to use that definition to indicate that patients are high risk when they are not, and that will turn influence selection criteria for these trials. Remember, chronic obstructive pulmonary disease is a couple of pulmonary diseases—airways disease and emphysema, 2 very different conditions, both with very different risk factors. The FEV_1 can be 25% with no emphysema because it's due to small airways disease, or it can be due to loss of elastic recoil, namely, emphysema. Diffusing capacity is a little different. A person with an FEV_1 of 25% whose computed tomography scan doesn't show much emphysema and whose diffusing capacity is 35% to 40% is not a particularly high-risk patient for a lobectomy if you choose well. In summary, FEV_1 alone does not adequately define risk for resection and potentially does a great disservice to patients. Furthermore, it ignores the importance of the surgeon's judgment and experience in selecting appropriate patients for surgical resection.

Dr Fernando. I will say that the American College of Chest Physicians in their guidelines used 80% for their cutoff for what defined high or low risk, and they also recommended more invasive evaluation of those patients, including split-lung ventilation/perfusion scans, which seems kind of ridiculous for patients with such a high FEV%. That's something that Frank Detterbeck is investigating in another study. I also think there is a real problem with trying to accrue patients to studies, and if we only used

a low FEV_1 cutoff point, we would have taken forever to do this, and perhaps not completed the study.

Dr Joachim Schirren *(Wiesbaden, Germany)*. I have 2 questions. First, you had a consensus conference about the surgical procedure from 9 centers? Second, why do you use DLCO? Currently, I think it's important to see the dynamics of the patient during spiroergometry. The last point is, if you have a patient with a DLCO that you described, you walk with him, 3 stairs, 4 stairs, and then you decide if you will operate. It would be interesting to see how the DLCO was, how the physiologic status was of the patient to steps, stairs, and, second, to see how the spiroergometry was. Can you say something about this?

Dr Fernando. We didn't use a stair-climbing test as such. Actually, I think it's 35 sites that participated. The sites listed were the top 5 accruing sites, plus some of the radiation staff who were involved in the study design and implementation. The way the trial developed is that we had a 2-day conference where we got together and reviewed what the best literature out there was. We invited some pulmonologists and radiation oncologists to the meeting as well. Then we broke off into groups to work out the optimal criteria that would define a high-risk group, as well as the optimal study for these patients. So this was worked out some time ago from that consensus conference. In fact, we used the same criteria for Z4033, which is the radiofrequency ablation study that also recently completed accrual. The only difference there was that the surgeon had to see the patient and state that he or she didn't think the patient was even a candidate for sublobar resection. As you can imagine, it took a lot longer to accrue patients to that 50-patient trial because many of these patients were probably treated with resection.